CLAIMS

1. A compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway.

2. A compound according to claim 1 for use as a medicament for the modulation of angiogenesis wherein said compound has its angiogenic effect via:
   - the modulation of the cholesterol metabolism and/or flux, and/or
   - the modulation of the caveolin-1 abundance/activity, and/or,
   - the modulation of the eNOS abundance/activity, and/or,
   - the modulation of the calmodulin abundance/activity, and/or,
   - the modulation of the Hsp90 abundance/activity, and/or,
   - the modulation of the NO production.

3. A compound according to claims 1 or 2 for use as a medicament for the modulation of angiogenesis, wherein said compound modulates intracellular free cholesterol by acting on cholesterol synthesis, cholesterol metabolism, cholesterol influx or cholesterol efflux.

4. A compound according to any of the claims 1 to 3 for use as a medicament for the modulation of angiogenesis, wherein said compound influences cholesterol metabolism and decreases caveolin-1 abundance and is chosen from the group comprising HMGCoA reductase inhibitors or a pharmacologically acceptable derivative thereof.

5. A compound according to claim 4 for use as a medicament for the modulation of angiogenesis wherein said HMGCoA reductase inhibitor is chosen from the group comprising atorvastatin, mevastatin, lovastatin, simvastatin, pravastatin, fluvastatin and cerivastatin.

6. A compound according to claim 4 for use as a medicament for the modulation of angiogenesis wherein said HMGCoA reductase inhibitor is preferentially atorvastatin.

7. A compound according to any of the claims 1 to 3 for use as a medicament for the modulation of angiogenesis, wherein said compound influences cholesterol metabolism and increases caveolin-1 abundance, is chosen from a group comprising ACAT inhibitors or a pharmacologically acceptable derivative thereof.

8. A compound according to claim 7 for use as a medicament for the modulation of angiogenesis wherein said ACAT inhibitor is chosen from the group comprising avasimibe, NTE122, compound 58-035, TS-962 and the bacterial product epicochlioquinone A.

9. A compound according to any of the claims 1 to 3 for use as a medicament for the modulation of angiogenesis wherein said compound increases the export of cholesterol out of peripheral cells through the increased abundance of HDL particles resulting in the modulation of caveolin-1.

10. A compound according to claim 9 for use as a medicament for the modulation of angiogenesis which is chosen from a group comprising fenofibrate, bezafibrate and ciprofibrate.

11. A compound according to any of the claims 1 to 3 for use as a medicament for the modulation of angiogenesis wherein said compound decreases the production of cholesterol-rich VLDL particles by the liver.

12. A compound according to claim 11 for use as a medicament for the modulation of angiogenesis is chosen from the group comprising nicotinic acid.

13. A compound according to any of the claims 1 to 2 for use as a medicament for the modulation of angiogenesis wherein said compound influences abundance and/or activity of caveolin-1, eNOS, Hsp90 or calmodulin.

14. A compound according to claim 13 for use as a medicament for the modulation of

binant calmodulin, recombinant Hsp90 or a pharmacologically acceptable derivative thereof.

15. A compound according to claim 13 for use as a medicament for the modulation of angiogenesis which is a nucleic acid encoding the partial or total amino acid sequence of caveolin-1 or an analogue thereof which can increase the caveolin-1 concentration in the cell thereby increasing the scavenging of the endogenous eNOS.

16. A compound according to claim 13 for use as a medicament for the modulation of angiogenesis which is a nucleic acid encoding the partial or total amino acid sequence of eNOS or an analogue thereof which can increase the eNOS concentration and/or activity in the cell thereby increasing the production of intacellular NO.

17. A compound according to claim 13 for use as a medicament for the modulation of angiogenesis, which is able to change the concentration of endogenous caveolin-1, eNOS, calmodulin or Hsp90.

18. A compound according to claim 17 for use as a medicament for the modulation of angiogenesis, being an antisense nucleic acid able to hybridise with a corresponding nucleotide sequence encoding the caveolin-1 and antagonizes the expression of the caveolin-1 protein in the cell.

19. A compound according to claim 18 for use as a medicament for the modulation of angiogenesis, being an antisense nucleic acid as defined by SEQ ID NO 5.

20. A compound according to claim 13 for use as a medicament for the modulation of angiogenesis which consists of an antagonist or agonist of caveolin-1, eNOS, calmodulin or Hsp90.

21. A compound according to claims 13 and 20 for use as a medicament for the modulation of angiogenesis, which is able to trap the endogenous caveolin-1 preventing

22. A compound according to claim 13 and 20 for use as a medicament for the modulation of angiogenesis which is a nucleic acid encoding the partial or total amino acid sequence of eNOS or the eNOS sequence deleted or mutated in the active caveolin binding site or an analogue thereof which can increase the concentration of unbound (activated) eNOS.

23. A compound according to claim 22 for use as a medicament for the modulation of angiogenesis wherein said trapping molecule comprises an amino acid sequence pattern as described in SEQ ID NO 4, preferably comprising the amino acid sequence pattern as described in SEQ ID NO 6 to SEQ ID NO 86.

24. A compound according to claim 13 for use as a medicament for the modulation of angiogenesis, which is able to trap the endogenous eNOS preventing the formation of NO.

25. A compound according to claim 24 for use as a medicament for the modulation of angiogenesis wherein said partial amino acid sequence comprising the caveolin-1 scaffolding domains A and/or B as described in SEQ ID NO 2 and SEQ ID NO 3 or portions thereof able to bind selectively upon the endothelial isoform of nitric oxide synthase (eNOS).

26. A compound according to claim 24 for use as a medicament for the modulation of angiogenesis which is a nucleotide sequence encoding the partial or total amino acid sequence of caveolin or an analogue which can be used to decrease the unbound (inactivated) eNOS concentration in the cell.

27. A pharmacological composition comprising a compound according to any of the claims 1 to 26 or a pharmacologically acceptable derivative thereof for the stimulation or inhibition of angiogenesis.

28. Use of a compound according to claims 1 to 26, optionally combined with a suitable excipient, for the treatment of angiogenesis related diseases such as angiogenesis-dependent tumour growth and metastatic diseases, ischemic heart and peripheral vascular diseases including cerebral diseases and wound healing.

29. Diagnostic kit for the testing of a compound or a composition for their ability to modulate angiogenesis via the intracellular free cholesterol-caveolin1-eNOS-NO pathway.

30. Method for screening compounds or compositions which modulate angiogenesis via the intracellular free cholesterol-caveolin1-eNOS-NO pathway.

31. Method to manufacture a medicament for the modulation of angiogenesis comprising a compound according to any of the claims 1 to 26.

32. Method of treating a subject in the need of influencing angiogenesis by administering an angiogenesis-modulating-compound according to claims 1 to 26 in a sufficient concentration able to modulate angiogenesis within this subject.

33. Use of a compound according to claims 1 to 26 for the modulation of the cholesterol metabolism in a cell in vitro, in vivo or ex vivo.

34. Use of a compound according to any of the claims 1 to 26 for the modulation of the expression of caveolin-1 in a cell in vitro, in vivo or ex vivo.

35. Use of a compound according to any of the claims 1 to 26 for the modulation of the expression of eNOS in a cell in vitro, in vivo or ex vivo.

36. Use of a compound according to any of the claims 1 to 26 for the modulation of the expression of calmodulin in a cell in vitro, in vivo or ex vivo.

37. Use of a compound according to any of the claims 1 to 26 for the modulation of the expression of Hsp90 in a cell in vitro, in vivo or ex vivo.